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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/805,290	03/13/2001	Sandra Bezemer	F7526(V)	1258

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/805,290	BEZEMER ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/12/05 & 5/9/05*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-12* is/are pending in the application.

4a) Of the above claim(s) *6-8,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 5/12/05 and Applicant's response filed 5/9/05 are acknowledged and have been entered.

2. Applicant is reminded of Applicant's election with traverse of Group I (claims 3-5), and species of SEQ ID NO: 8 as the CDR3 species and SEQ ID NO: 19 as the antibody/fragment in Applicant's response filed 7/21/04.

Claims 6-8, 11 and 12 (non-elected Groups II-VI) are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions. (It is noted by the Examiner that withdrawn claim 6 depends upon a canceled claim, withdrawn claim 7 depends upon claim 6, and withdrawn claim 8 depends upon claim 7).

Applicant is reminded that upon consideration of a search of the prior art, the search had been extended to include SEQ ID NO: 8-26.

Claims 1, 3-5, 9 and 10 are currently being examined.

The following are new grounds of rejection necessitated by Applicant's amendment filed 5/12/05.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 3-5, 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of: (1) the claimed antibody that binds specifically to more than one human dietary lipase and wherein the antibody or fragment thereof of comprises a V_HH, and food product or pharmaceutical, recited in the instant claims, (2) the claimed antibody recited in instant claim 4 wherein the antibody or fragment thereof that binds one or more

human dietary lipases comprises 3 CDR regions, whereby CDR3 is one of the recited SEQ ID NO and wherein the antibody or fragment thereof of comprises a V_HH, and the antibody or fragment thereof is not one of the full length antibody sequences or antigen binding fragments thereof of the SEQ ID NO recited in instant claim 5.

The instant claims encompass: (1) an antibody/fragment thereof/ and pharmaceutical or food composition thereof that is capable of binding specifically to more than one of the human dietary lipases that have very different sequences, wherein the antibody or fragment comprises a V_HH, (2) an antibody or fragment thereof that specifically binds human pancreatic lipase and comprises a CDR3 from the sequences recited in instant claim 4 and has undisclosed other portions. There is insufficient disclosure in the specification on such an antibody/fragment/functional equivalent/composition thereof wherein the antibody or fragment comprises a V_HH.

The specification discloses that it is desirable to decrease the level of LDL and that several dietary enzymes may be involved in the hydrolysis reaction that liberates fatty acids in the GI tract to increase the adsorption of cholesterol by the epithelium (page 1). The specification discloses that other enzymes in the GI tract may be involved in undesirable physiological reactions and examples of such enzymes, referred to as human dietary enzymes, include oxidoreductases, transferases, hydrolases (e.g. lipases, proteolytic enzymes and ureases), lyases, isomerases and ligases or synthetases (page 2 at lines 1-5). The specification discloses that human pancreatic lipase (HPL) was purified, used as an immunogen to generate V_HH antibodies in a llama, and V_HH fragments that inhibited HPL were cloned, selected, screened, enriched, a portion were sequenced, and the V_HH were grouped into three classes depending upon the length of CDR3 which is the most important region for binding to the antigen (pages 15-24). The specification further discloses that a number of these were re-cloned and purified (pages 25-26). The specification discloses parallel work for production of V_HH antibodies to human gastric lipase (HGL) (pages 28-32). The specification discloses feeding the antibodies HPL18 and HGL8 to piglets in combination with a high fat diet, and that in 2/3 animals, the antibodies inhibited fat digestion and uptake as evidenced by a reduction in blood triglyceride levels (pages 33-36). The specification further discloses that the V_HH antibodies are used for the inhibition, or in the case of human dietary lipases for partial inhibition, of the enzymes involved in the hydrolysis of dietary fats (pages 8 at lines 28-31, page 9 at lines 23-30 and the brief description of the drawings for Figures 1-3, figures 1-3).

The specification does not disclose antibodies that are capable of binding specifically to more than one human dietary lipase, including the antibodies exemplified in the specification, nor does the specification disclose such antibodies comprising just the CDR3 regions peptides recited in instant claim 4 without the corresponding other CDR1 and CDR2 regions that accompany them in the intact antibody or antigen binding fragment thereof of the SEQ ID NO recited in instant claim 5. The instant specification does not disclose which portions or features of human dietary lipases are important for

functional activity of the said lipases, if there are regions of identity between the functionally relevant portions of the said lipases for which one antibody is required to specifically bind to more than one of the said lipases. The specification does not disclose what amino acid sequences or combination of sequences makes a dietary lipase "human".

Evidentiary reference Lowe et al (J. Biol. Chem. 264(33): 20042-20048, 1989, IDS reference) teaches that human gastric lipase has only 4% homology with human pancreatic lipase, i.e., an example of enzymes with lipase function but with significantly different sequences.

There is no description in the specification as to what alterations result in a functional antibody or fragment thereof that binds specifically to more than one human dietary lipase, or a functional antibody or fragment thereof that binds specifically to human pancreatic lipase and comprises the SEQ ID NO recited in instant claim 4, except for the antibodies or antigen binding fragments thereof of the SEQ ID NO recited in instant claim 5.

The recitation in the instant claims does not specifically define any of the compounds that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others, other than that they are antibodies or antigen binding fragments thereof that bind specifically to one or more proteins of undisclosed structure and which have a functional activity of being a "human dietary lipase" or a "human pancreatic lipase". One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. In addition, a definition by function does not suffice to define the genus because it is only an indication of what the property the human dietary lipase(s) has that the antibody or antigen binding fragment binds to, and if one extends the analysis in the instant case, what the enzyme does rather than what it is, i.e., it hydrolyzes dietary fats. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many such species may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

The instant disclosure does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. Since the disclosure fails to provide sufficient relevant identifying characteristics, and because the genus is highly

variant, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

5. Claims 1, 3-5, 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not disclose how to make and/or use the instant invention: (1) the claimed antibody that binds specifically to more than one human dietary lipase and wherein the antibody or fragment thereof of comprises a V_HH, and food product or pharmaceutical, recited in the instant claims, (2) the claimed antibody recited in instant claim 4 wherein the antibody or fragment thereof that binds one or more human dietary lipases comprises 3 CDR regions, whereby CDR3 is one of the recited SEQ ID NO and wherein the antibody or fragment thereof of comprises a V_HH, and the antibody or fragment thereof is not one of the full length antibody sequences or antigen binding fragments thereof of the SEQ ID NO recited in instant claim 5.
The specification has not enabled the breadth of the claimed invention because the claims encompass: (1) an antibody/fragment thereof/ and pharmaceutical or food composition thereof that is capable of binding specifically to more than one of the human dietary lipases that have very different sequences, wherein the antibody or fragment comprises a V_HH, (2) an antibody or fragment thereof that specifically binds human pancreatic lipase and comprises a CDR3 from the sequences recited in instant claim 4 and has undisclosed other portions. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed antibody/fragment and food product and composition thereof wherein the antibody or fragment comprises a V_HH can be made and/or used.

The specification discloses that it is desirable to decrease the level of LDL and that several dietary enzymes may be involved in the hydrolysis reaction that liberates fatty acids in the GI tract to increase the adsorption of cholesterol the epithelium (page 1). The specification discloses that examples of such enzymes, referred to as human dietary enzymes, include oxidoreductases, transferases, hydrolases (*e.g.,* lipases, proteolytic enzymes and ureases), lyases, isomerases and ligases or synthetases (page 2 at lines 1-5). The specification discloses that human pancreatic lipase (HPL) was purified, used as an immunogen to generate V_HH antibodies in a llama, and V_HH fragments that inhibited HPL were cloned, selected, screened, enriched, a portion were sequenced, and the V_HH were grouped into three classes depending upon the length of CDR3 which is the most important region for binding to the antigen (pages 15-24). The specification further discloses that a number of these were re-cloned and purified (pages 25-26). The specification discloses parallel work for production of V_HH antibodies to human gastric lipase (HGL) (pages 28-32). The specification discloses feeding the antibodies HPL18 and HGL8 to piglets in combination with a high fat diet, and that in 2/3 animals, the antibodies inhibited fat digestion and uptake as evidenced

by a reduction in blood triglyceride levels (pages 33-36). The specification further discloses that the V_HH antibodies are used for the inhibition, or in the case of human dietary lipases for partial inhibition, of the enzymes involved in the hydrolysis of dietary fats (pages 8 at lines 28-31, page 9 at lines 23-30 and the brief description of the drawings for Figures 1-3, figures 1-3).

Evidentiary reference Lowe et al (J. Biol. Chem. 264(33): 20042-20048, 1989, IDS reference) teaches that human gastric lipase has only 4% homology with human pancreatic lipase, i.e., an example of enzymes with lipase function but with significantly different sequences.

The specification does not disclose antibodies that are capable of binding specifically to more than one human dietary lipase, including the antibodies exemplified in the specification, nor does the specification disclose making such antibodies starting from just the CDR3 regions peptides recited in instant claim 4. The instant specification does not disclose which portions or features of human dietary lipases are important for functional activity of the said lipases, if there are regions of identity between the functionally relevant portions of the said lipases for which one antibody is required to specifically bind to more than one of the said lipases, and hence it is unpredictable if the antibodies can be made and/or used.

There is no guidance in the specification as to what alterations result in a functional antibody or fragment thereof that binds specifically to more than one human dietary lipase, or a functional antibody or fragment thereof that binds specifically to human pancreatic lipase and comprises the SEQ ID NO recited in instant claim 4. Because of this lack of guidance, the extended experimentation that would be required to determine which additions would be acceptable to retain functional activity of binding specifically to human pancreatic lipase or to confer cross-reactive binding to more than one human dietary lipase, especially as the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e., its activity) are not well understood and are therefore not predictable (Ngo et al. The Protein Folding Problem and Tertiary Structure Prediction, Merz & LeGrand, Birkhauser Boston, pages 491-495, 1994, entire article, especially Section 6, paragraph 1, of record), it would require undue experimentation for one of skill in the art to arrive at other amino acid sequences that would have functional activity. In other words, since it would require undue experimentation to identify amino acid sequences that have functional activity, it would require undue experimentation to make and use the corresponding sequences.

There is insufficient guidance in the specification as to how to make and/or use instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is indefinite in the recitation of "and wherein X3 is selected from the group of V or L or I" because a proper Markush Group recites "selected from the group consisting of V, L and I". It is suggested that Applicant amend said claim to properly recite the Markush Group.

8. It is noted by the Examiner that claim 3 contains a typographical error, "of fragment thereof" which should be "or fragment thereof" in line 1, and "Human" is capitalized and should be "human". (Withdrawn claim 6 also contains the same typographical error at line 1). It is noted by the Examiner that claims 9 and 10 recite "in accordance to" whereas claim 3 recites "in accordance with". Applicant may wish to amend claims 9 and 10 for consistency.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 3, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/34630 (IDS reference) in view of Aoubala et al (J. Biol. Chem. 8: 3932-3937, 1995, IDS reference), STN Accession Number: 1998286804 EMBASE , WO 99/46300 (IDS reference) and U.S. Patent No. 6,558,936 B1.

WO 98/34630 teaches use of a gastrointestinal lipase inhibitor in oral medicaments for treating type II diabetes mellitus and for the control of obesity and hyperlipidemia.

WO 98/34630 does not teach medicaments comprising an antibody, or fragment thereof, capable of binding specifically to one or more human dietary enzymes, said antibody or fragment thereof comprising a V_HH, nor wherein the antibody or fragment thereof or functional equivalent is capable of specifically binding human pancreatic lipase (HPL).

Aoubala et al teach anti-HPL mAbs that inhibit the lipolytic activity of HPL.

STN Accession Number: 1998286804 EMBASE teaches that inhibition of pancreatic lipase offers the opportunity to intensify the weight reducing effect of diet, and that obesity increases risk of type II diabetes mellitus.

WO 99/46300 teaches that V_HHs are comparable to mouse monoclonal antibodies in terms of specificity, high affinity but are more stable against destabilizing physical and/or chemical conditions, including under pasteurization conditions, than traditional antibodies and that it is therefore advantageous to use them in food products. WO 99/46300 teaches food products include ice cream, oils, margarines, dressings, drinks and meals. WO 99/46300 teaches that V_HHs have superior stability, specificity and affinity as compared to mouse mAbs, characteristics that make them excellent candidates for use in existing and novel applications. WO 99/46300 teaches that V_HHs can be produced that bind specifically to and neutralize enzymes that are present (especially page 20). WO 99/46300 teaches methods of making V_HHs (see entire document).

U.S. Patent No. 6,558,936 B1 discloses use of antagonists, including antibodies in therapeutic pharmaceutical compositions to inhibit the activity of a lipase protein. U.S. Patent No. 6,558,936 B1 further discloses that dietary lipids are taken up primarily by hydrolysis of fatty acyl moieties from their corresponding polyol moiety and this reaction is catalyzed by lipases, followed by diffusion across the gut wall (especially column 1 at lines 16-42). U.S. Patent No. 6,558,936 B1 discloses that antibodies to the said lipase protein, and disclose that said lipase protein has activity similar or identical to human pancreatic lipase, are useful for treating hyperlipidemia, atherosclerosis, diabetes and obesity (especially column 3 at lines 45-64, column 10 at lines 55-63, column 48 at lines 42-69, and columns 49 and 50).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a V_HH version of a neutralizing anti-enzyme V_HH antibody as taught by WO 99/46300 with the specificity of an anti-human pancreatic lipase (anti-HPL) antibody such as that taught by Aoubala et al in the oral pharmaceutical composition taught by WO 98/34630 or a food product such as taught by WO 99/46300 to inhibit pancreatic lipase as taught by WO 98/34630, STN Accession Number: 1998286804 EMBASE and by U.S. Patent No. 6,558,936 B1 for pancreatic lipase.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to treat obesity and/or diabetes mellitus type II as taught by WO 98/34630 and by STN Accession Number: 1998286804 EMBASE using a more stable version of the neutralizing anti-HPL mAbs taught by Aoubala et al such as the V_HHs taught by WO 99/46300 since WO 99/46300 teaches the advantage of using them in food products. With regard to the inclusion of claim 10 in this rejection, the combined invention is a pharmaceutical product since it is being administered to a subject *in vivo*.

Applicant's arguments in Applicant's said amendment and response filed 5/12/05 and 5/9/05, respectively, have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's said amendment and response beginning on page 2 of Applicant's said response.

It is the Examiner's position with regard to Applicant's argument that it is unclear that there is any disclosure or suggestion given by Aoubala et al that the types of antibodies of the present invention would have any effect against human dietary lipase, that human pancreatic lipase is a human dietary lipase, as disclosed in the instant specification on page 7 at lines 5-8 and at lines 20-32, i.e., "human dietary enzymes, in particular enzymes involved in the hydrolysis of dietary fats" and "Human Pancreatic Lipase (HPL) is the major lipase responsible for lipid conversion in adults", and as recited in dependent claim 3, so the neutralizing antibodies prepared against human pancreatic lipase taught by Aoubala et al would be expected to have an effect against "human dietary lipase". It is the Examiner's further position with regard to Applicant's arguments to the STN reference that the STN reference cited above is being argued separately by Applicant. It is the Examiner's position with regard to Applicant's argument that it is unclear that WO 99/46300 has any disclosure of the ability of the antibodies to bind to human dietary lipases or that such antibodies would be effective against such lipases or that they could be used to inhibit the lipases to aid in reduction of dietary fats, that the WO 99/46300 is being argued separately. WO 99/46300 teaches that V_HHs are comparable to mouse monoclonal antibodies in specificity of binding and affinity, and that neutralizing V_HHs may be made that possess specificity for enzymes, but that V_HHs are superior to mouse monoclonal antibodies and are particularly useful in food products. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in producing a neutralizing V_HH antibody against HPL because the said WO document teaches comparable specificity and affinity of binding and that neutralizing V_HHs against enzymes can be produced, and Aoubala et al teach neutralizing monoclonal antibodies against HPL. It is the Examiner's position with regard to Applicant's argument that it is not apparent that there is any teaching by US 6,558,936 concerning the possibility of using the antibodies of the invention to bind with human dietary lipases and so to provide the advantages provided by the present invention, that US 6,558,936 teaches antibodies that inhibit pancreatic lipase said lipase having similar or identical activity to human pancreatic lipase. Further, the reference is not relied upon for use of those specific antibodies, but rather for the disclosure of inhibition of pancreatic lipase using an antibody, and Aoubala et al are relied upon for the teaching of neutralizing antibodies to HPL. In addition, the pancreatic lipase disclosed by US 6,558,936 is also a "human dietary lipase" according to Applicant's definition in the specification. It is the Examiner's position that WO 99/46300 and Aoubala et al are being argued separately with regard to Applicant's argument that one teaches V_HH antibodies but not against human dietary lipases, while the other teaches monoclonal antibodies against human pancreatic lipases but not V_HH antibodies, that combination of both would result in the opposite expectation and that there is no clear

motivation to produce a V_HH version of an inhibiting anti-HPL antibody based on the combination of the two references because it is not clear that there would be any expectation of success. It is the Examiner's position that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed method as enunciated in the instant rejection and in the Examiner's position herein.

With regard to Applicant's arguments as to the number of references (i.e., 5) cited in the instant invention, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

11. Claims 1, 3, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,558,936 B1 in view of Aoubala et al (J. Biol. Chem. 8: 3932-3937, 1995, IDS reference) and WO 99/46300 (IDS reference).

U.S. Patent No. 6,558,936 B1 discloses use of antagonists, including antibodies in therapeutic pharmaceutical compositions to inhibit the activity of a lipase protein. U.S. Patent No. 6,558,936 B1 further discloses that dietary lipids are taken up primarily by hydrolysis of fatty acyl moieties from their corresponding polyol moiety and this reaction is catalyzed by lipases, followed by diffusion across the gut wall (especially column 1 at lines 16-42). U.S. Patent No. 6,558,936 B1 discloses that antibodies to the said lipase protein are useful for treating hyperlipidemia, atherosclerosis, diabetes and obesity (especially column 3 at lines 45-64, column 48 at lines 42-69 and columns 49 and 50).

U.S. Patent No. 6,558,936 B1 does not disclose a pharmaceutical or food composition comprising an antibody, or fragment thereof, capable of binding specifically to one or more human dietary enzymes, said antibody or fragment thereof comprising a V_HH, nor wherein the antibody or fragment thereof or functional equivalent is capable of specifically binding human pancreatic lipase (HPL).

Aoubala et al teach anti-HPL mAbs that inhibit the lipolytic activity of HPL.

WO 99/46300 teaches that V_HHs are more stable against destabilizing physical and/or chemical conditions, including under pasteurization conditions, than traditional antibodies and that it is therefore advantageous to use them in food products. WO 99/46300 teaches food products include ice cream, oils, margarines, dressings, drinks and meals. WO 99/46300 teaches that V_HHs have superior stability, specificity and affinity as compared to mouse mAbs, characteristics that make them excellent candidates for use in existing and novel applications.
WO 99/46300 teaches methods of making V_HHs.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a V_HH version as taught by WO 99/46300 of an inhibiting anti-HPL antibody such as that taught by Aoubala et al in the pharmaceutical

composition disclosed by U.S. Patent No. 6,558,936 B1 to inhibit pancreatic lipase as disclosed by U.S. Patent No. 6,558,936 B1 for another pancreatic lipase.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to treat obesity and/or diabetes mellitus type II as taught by U.S. Patent No. 6,558,936 B1 using a more stable version of the neutralizing anti-HPL mAbs taught by Aoubala et al such as the V_HHs taught by WO 99/46300 since WO 99/46300 teaches the advantage of using them include higher stability and affinity, particularly under destabilizing conditions. With regard to the inclusion of claim 9 in this rejection, WO 99/46300 teaches the advantage of using V_HHs in food preparations, and since U.S. Patent No. 6,558,936 B1 discloses the first site of lipase action is in the lumen of the gut, it would have been obvious to include the antibody in an oral pharmaceutical preparation or a food product such as those taught by WO 99/46300 for use with other V_HHs.

Applicant's arguments in Applicant's said amendment and response filed 5/12/05 and 5/9/05, respectively, have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's said amendment and response beginning on page 4 of Applicant's said response, and are briefly the same as for the rejection preceding the instant rejection, that the combination of the teachings of the references would not render the present invention obvious to one of ordinary skill in the art.

The Examiner's position in the rejection prior to the instant rejection applies herein as it pertains to the references cited in the instant rejection.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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